AF 1634

ARNOLD & PORTER LLP

Thomas E. Holsten
Thomas_Holsten@aporter.com

202.942.5085
202.942.5999 Fax

555 Twelfth Street, NW
Washington, DC 20004-1206

May 6, 2005

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Art Unit: 1634
Examiner: Sarae L. Bausch
Conf. No.: 6793

Re: U.S. Patent Application No. 09/912,968 filed July 25, 2001
Inventors: Stanton B. DOTSON *et al.*
Title: A Method for Assessing Transgene Expression and Copy Number
Atty. Dkt: 16517.275

Sir:

Transmitted herewith for appropriate action by the U.S. Patent and Trademark Office (PTO) are the following documents:

1. Appellant's Brief, with attached Appendix A; and
2. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier.

Authorization is hereby given to charge the statutory fee of $500.00 for filing Appellants' Brief to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.275. A duplicate copy of this letter is enclosed.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Appellants do not believe any additional fees are due in conjunction with this filing. However, if any fees are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.275. A duplicate copy of this letter is enclosed.

Respectfully submitted,

Thomas E. Holsten (Reg. No. 46,098)

Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:	Confirmation No.: 6793
Stanton B. DOTSON *et al.*	Art Unit: 1634
Appln. No.: 09/912,968	Examiner: Sarae L. Bausch
Filed: July 25, 2001	Atty. Docket: 16517.275

For: **A Method for Assessing Transgene Expression and Copy Number**

APPELLANT'S BRIEF

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-captioned patent application. A Notice of Appeal was filed on February 7, 2005. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter.

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant is unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 35-50 are pending. Claims 1-34 were cancelled without prejudice to or disclaimer of the subject matter claimed therein in a Preliminary Amendment filed April

12, 2002[1]. Claim 50 stands finally rejected under 35 U.S.C. §§ 112, first paragraph, claims 35, 41, 47, and 49 stand finally rejected under 35 U.S.C. § 102(b) and claims 35-39 and 41-50 stand finally rejected under 35 U.S.C. § 103(a). Appellant appeals all of the rejections of claims 35-39 and 41-50.

4. Status of Amendments

Appellant has not filed any responses subsequent to Final Rejection in this case.

5. Summary of Claimed Subject Matter

The claimed subject matter is directed to a method to detect expression of a first transgenic nucleic acid molecule in a sample having either (a) a detectable amount of mRNA transcribed from a second transgenic nucleic acid molecule or (b) a substantially non-detectable amount of the mRNA, the method comprising providing a complementary DNA of the mRNA, amplifying the complementary DNA and hybridizing the complementary DNA with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule whereby the hybridizing indicates the expression of the first transgenic nucleic acid molecule in a sample.. Specification at page 4, line 21 through page 6, line 2; page 28, line 21 through page 37, line 9; and the claims as originally filed. The claimed subject matter is also directed to a amplification kit for the detection of a transgenic nucleic acid molecule comprising at least one primer pair and a corresponding labeled probe which hybridizes under stringent hybridization conditions to a nucleic acid molecule of a 3' end of the *Pisum sativum* rbcS E9 gene. Specification at page 36, lines 16-32; page 12, line 2 through page 13, line 18; and claims as originally filed. A copy of the claims on appeal is attached hereto as Appendix A.

---

[1] Appellant notes that the claims submitted in the Preliminary Amendment filed on April 12, 2002 were renumbered as 35-50. *See*, Office Action mailed August 26, 2003 at page 2.

6. Grounds of Rejection to be Reviewed on Appeal

The grounds of rejection to be reviewed in this Appeal are:

(a) pending claim 50 stands rejected under 35 U.S.C. § 112, first paragraph for alleged insufficient written description;

(b) pending claims 35, 41, 47, and 49 stand rejected under 35 U.S.C. § 102(b) for alleged anticipation; and

(b) pending claims 35-39 and 41-50 stand rejected under 35 U.S.C. § 103(a) for alleged obviousness.

7. Argument

A. Summary of Appellant's Position

Appellant has provided a description of the claimed amplification kit that demonstrates Appellant's possession of the claimed invention. The genera of nucleic acid sequences that hybridize under stringent hybridization conditions to a nucleic acid molecule of a 3' end of the *Pisum sativum* rbcS E9 gene, have been fully described by the recitation of common structural features, *e.g.*, the nucleotide sequence of SEQ ID NO: 2, which distinguishes molecules in the claimed genera from molecules not in the claimed genera. Because the specification demonstrates that Applicants had possession of, and have provided an adequate description of, the claimed genera of nucleic acid molecules, the specification satisfies the written description requirement of 35 U.S.C. § 112.

The claimed nucleic acid molecules are novel and non-obvious over the prior art. The claims are directed to methods to detect the expression of a first nucleic acid molecule in sample employing hybridizing a complementary DNA of an mRNA from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in a sample. The references cited by the Examiner do not disclose, teach or even suggest the claims of the present

invention. Absent a disclosure, teaching or suggestion of each and every element of the claims, *i.e.*, methods to detect the expression of a first nucleic acid molecule in sample employing hybridizing a complementary DNA of an mRNA from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in a sample, the references cited by the Examiner does not anticipate or obviate the present claims.

B. The Specification Provides An Adequate Written Description of the Claimed Invention

The adequacy of the written description of claim 50 has been challenged by the Examiner because the claim allegedly "contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Final Action at pages 3-7.

The Examiner's rejection is premised on two grounds. First, the Examiner argues that the Appellant's amendment of claim 50 to recite "hybridizes under stringent conditions" allegedly "allows for polynucleotides with substantial variation with regard to 3' end of the *Pisum sativum* rbcS E9 gene" that were not described in the specification. Final Action at pages 3-5. In addition, the Examiner maintains that "[C]laim 50 encompasses any sequences that are at most described as the 3'-untranslated sequence from the 3' end of the *Pisum sativum* rbcS E9 gene" and the "specification provides insufficient written description to support the genus encompassed by the claims." Office Action mailed March 22, 2004 at page 3.

Initially, Appellant notes that one of bases for the Examiner rejections appears to depend on the open claim language recited in the claims. This is not a proper basis for a written description rejection of a "comprising" claim. If it were, every "comprising"

claim ever written would be invalid for failing to describe every nuance of the claimed invention. Furthermore, the specification demonstrates to one skilled in the art that Appellant was in possession of the claimed genera of nucleic acid molecules.

(1) The Specification Reflects Applicants' Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventor had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Appellant need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989). A related, and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985), *quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981). Thus, simply because the claimed nucleic acid sequences may also include sequences from "other species, mutated fragment sequences, allelic variants, splice variants, genomic sequences and so forth" does not require that Applicants describe each and every one of these molecules.

Furthermore, if a person of ordinary skill in the art would, after reading the specification, understand that the inventor had possession of the claimed invention, even if not every nuance, then the written description requirement has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. A person of ordinary skill in the art would, after reading the present specification, understand that Applicants had possession of the claimed invention.

For example, the specification describes gene sequences, corresponding sequences preferred sequences, and so forth of the *Pisum sativum* rbcS E9 gene (*see, e.g.,* specification at page 26, line 1 through page 28, line 14; in the Sequence Listing; and in the claims as originally filed). The specification also describes appropriate hybridization conditions, including (*see, e.g.,* specification at page 12, line 12 through page 13, line 18); oligonucleotides and primers for obtaining oligonucleotides (*see, e.g.*, specification at page 9, line 22 through page 10, line 24 and in the sequence listing); oligonucleotides that hybridize to 3' untranslated regions (*see, e.g.* specification at page 21, line 17 through page 22, line 4 and in the sequence listing); and expression detection and quantitation methods (*see, e.g.*, specification at page 28, line 15 through page 37, line 9). Despite the numerous variations described for the nucleic acid molecules in the present specification, the Examiner argues that "[w]ith the exception of SEQ ID NOs: 2, 7-9, and 28 the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides." Office Action at page 5.

The written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...*i.e.,* complete or partial structure, other physical and or chemical properties, functional char-

acteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002). (quoting from Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001)). Appellant has satisfied that test for written description. For example, Appellant has disclosed a structural feature, the nucleotide sequence of SEQ ID NO: 2. This feature provides a basis for each and every nucleic acid molecule in the claimed genus. Moreover, it distinguishes the members of the claimed genus from non-members. In addition, the specification discloses that such sequence is from the 3' untranslated region of the *Pisum sativum* rbcS E9 gene. Furthermore, as described above, the specification discloses sufficient description of hybridization conditions to allow a skilled artisan to recognize members of the claimed genus from non-members.

In light of the detailed disclosure of the present application, one skilled in the art, after reading the present specification, would clearly know if a nucleic acid molecule contains one of the recited nucleotide sequences. Thus, pending claim 50 is supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, and the rejection should be reversed.

C. The Claimed Methods Are Novel

The novelty of the claimed invention has been challenged by the Examiner under 35 U.S.C. §102(a) because claims 35, 41, 47, and 49 are allegedly anticipated by Hamilton *et al.* Final Action at page 7-9. "It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal*

Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Further, "an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device." *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q. 619 (Fed. Cir. 1985). The identical invention must be shown in complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989). Nothing in the cited reference discloses the claimed invention.

In support of this rejection, the Examiner asserts that: "Hamilton demonstrates the expression of transgenes in a BIBAC vector (p. 113, 2nd column, 3rd paragraph), wherein a successful transfection into the host plant is determined based upon the following transgenic nucleic acids: *sacB* gene, GUS-NPTII gene (beta-glucuronidase – neomycin phosphotransferase II), and the HYP gene (hygromycin phosphotransferase)." Office Action, at page 8.

The Hamilton *et al.* disclosure does not include all of the limitations of the present claims. The language that the Examiner recites from page 113 of Hamilton indicating that "[p]lants that tested positive for the BIBAC T-DNA by PCR were all verified by Southern analysis using a NPTII specific probe" does not indicate whether such sequences are expressed. Office Action at pages 8-9 (emphasis added).

Furthermore, the Examiner also relies on figure 4 to support the rejection. More specifically, the Examiner argues that "Hamilton demonstrates in figure 4b and c shows the hybridization of BIBAC DNA to a GUS-NPTII-specific probe and a HYG-specific probe, respectively." Final Action at page 9. Appellant submits that the description of figure 4 indicates that it demonstrates the "Southern analysis of BIBAC plasmids in *E. coli* and *A. tumefaciens*." Hamilton, *et al.* at page 114, Fig. 4. Again, nothing the Examiner points to indicates that such methods determine whether the sequences are expressed. Whatever else Hamilton *et al.* teaches, it does not disclose a method to detect the expression of a first nucleic acid molecule in sample employing hybridizing a complementary DNA of an

mRNA from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in a sample. Absent a teaching of each and every element of the claims, the reference cited by the Examiner does not anticipate claims 35, 36, 40-42 and 44-47 and the rejection should be reversed.

As such, the Examiner has failed to demonstrate that the reference discloses a method to detect the expression of a first nucleic acid molecule in sample employing hybridizing a complementary DNA of an mRNA from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in a sample and thus the rejection of pending claims 35, 41, 47, and 49 under 35 U.S.C. § 102(b) over Hamilton, *et al.* must be reversed.

D. The Claimed Methods Are Not Obvious

Claims 35-39 and 41-50 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hunt *et al.* (*DNA*, 1988), taken in combination with Freeman *et al.* (*BioTechniques*, 1999).

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not be based on Applicant's disclosure. *See* M.P.E.P. §§2143.01 and 2143.03.

In a proper obviousness determination, the changes from the prior art must be evaluated in terms of the whole invention, including whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the claimed invention. *See In re Chu,* 36 U.S.P.Q.2d 1089, 1094 (Fed. Cir. 1995). This includes what could be characterized as simple changes. *See, e.g., In re Gordon*, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984) (Although a prior art device could have been turned upside down, that did not make the modification obvious unless the prior art fairly suggested the desirability of turning the device upside down.).

Only when the prior art teaches or suggests the claimed invention does the burden fall on the applicant to rebut that *prima facie* case. *See In re Dillon,* 16 U.S.P.Q.2d 1897, 1901 (Fed. Cir. 1990) (in banc), *cert. denied,* 500 U.S. 904 (1991). However, a *prima facie* case of obviousness may be rebutted by showing that the art, in any material respect, teaches away from the claimed invention.

The present invention is drawn to methods to detect expression of a first transgenic nucleic acid molecule in a sample having either (a) a detectable amount of mRNA transcribed from a second transgenic nucleic acid molecule or (b) a substantially non-detectable amount of the mRNA, the method comprising providing a complementary DNA of the mRNA, amplifying the complementary DNA and hybridizing the complementary DNA with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridizing indicates the expression of the first transgenic nucleic acid molecule in a sample.

(1) The cited references do not teach or suggest all of the elements

The Examiner argues that Hunt *et al.* discloses "the transformation of a tobacco plant with a plasmid carrying the 3' noncoding strand of the pea rbcS-E9 3' region (claims 37, 38) which aligns 99.5% with SEQ ID NO: 2 (a 637 bp sequence) from residue 1-633

(claim 39), and a desired transgene pAH10 (figure 2A)." Office Action at page 10. The Examiner notes that Hunt *et al.*, however, "does not teach the amplification by PCR or RT-PCR, quantitative and competitive RT-PCR, the primers utilized for the amplification as required by claims 36, 41, 42, 47, 48 and 50." Office Action at page 11.

The Examiner further argues that "Freeman teaches the benefits of PCR, specifically utilizing quantitative RT-PCR, both competitive and non-competitive (pp. 116-117) to quantify mRNA (claims 36, 41, 42)." Office Action at page 11. The cited references do not disclose or suggest a method to detect the expression of a first transgenic nucleic acid molecule in a sample comprising amplifying a complementary DNA from an mRNA from a second transgenic nucleic acid molecule and hybridizing the cDNA with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where hybridizing indicates the expression of the first transgenic nucleic acid molecule in a sample.

The Examiner has stated that "it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the detection method of Hunt et al and further modify the mRNA expression analysis to utilize quantitative RT-PCR which includes amplification along with primers and probes designed for quantitative RT-PCR as per the teachings of Freeman et al. because Freeman teaches that quantitative RT-PCR provides increased sensitivity in mRNA detection." Office Action at page 11.

Initially, Applicants respectfully disagree with the Examiner's characterization of the art. By way of example, the Examiner asserts that "it would have been prima facie obvious ... to improve the detection method of Hunt, *et al*...." In this regard, Applicants note that nowhere does Hunt *et al.* disclose or suggest a method for detecting the expression of a first transgenic nucleic acid molecule. Hunt *et al.* does, however, provide an identification and characterization of cryptic polyadenylation sites in the 3' region of a pea *rbcS*-E9 gene. As such, it is respectfully submitted that the Examiner's conclusion of obviousness is based on improper reasoning and a misinterpretation of the art.

Even assuming *arguendo* that the combination is proper, the combination does not render the claimed invention obvious. Whatever else Hunt *et al.* and Freeman *et al.* disclose, the do not teach or suggest a method to detect the expression of a first transgenic nucleic acid molecule in a sample by hybridizing a complementary DNA of mRNA transcribed from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in the sample. The Examiner has not pointed to any specific suggestion in any of the cited references to reach the presently claimed invention.

The mere fact that references can be modified does not render the resultant modification obvious unless the prior art also suggests the desirability of the modification. M.P.E.P. § 2143.01; *In re Mills*, 16 U.S.P.Q.2d 1430, 1432 (Fed. Cir. 1990); *see also*, *In re Fritch*, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992). This includes what could be characterized as simple changes. *See*, *Gordon*, 221 U.S.P.Q. at 1127. Even changes that are allegedly "merely a matter of engineering design choice" require a suggestion of desirability in the prior art. *See*, *In re Kuhle*, 188 U.S.P.Q. 7, 9 (CCPA 1975). In *Kuhle*, the element in question as the "obvious matter of design choice" was obvious because it was "notoriously old with the common flashlight." *Id.* at 8. As such, the prior art did contain a teaching that suggested the modification in question to one of ordinary skill in the art, thereby establishing a *prima facie* case of obviousness.

In the present case, the deficiencies in the teachings of Hunt *et al.* regarding the "amplification by PCR or RT-PCR, quantitative and competitive RT-PCR, [and] the primers utilized for the amplification" are not compensated for by any other reference. As such, Hunt *et al.* does not provide specific motivation to one of ordinary skill in the art such that the skilled artisan would arrive at the present invention upon reading Rodriguez-Tome *et al.*

It is impermissible hindsight to find it obvious for one skilled in the art to combine the cited references to reach the invention in the present application absent some suggestion or motivation in the cited references. Therefore, it would not be obvious to one skilled in the art, from reading Hunt *et al.* and Freeman *et al.* that one could obtain the methods of the present invention.

Moreover, the skilled artisan would not turn to Hunt *et al.* to solve the problem of detecting the expression of a first transgenic nucleic acid molecule. "In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). *See also In re Deminski*, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986); *In re Clay*, 966 F.2d 656, 23 USPQ2d 1058 (Fed. Cir. 1992). Applicants submit that Hunt *et al.* is not analogous art. First, the Hunt *et al.* reference is not in the Applicant's field of endeavor. The Hunt *et al.* reference describes the identification of "a number of discrete, cryptic polyadenylation sites located downstream from the previously-determined poly(A) sites of" the 3' region of the pea *rbcS*-E9 gene. This is a different field of endeavor from the methods for detecting the expression of a first transgenic nucleic acid molecule in a sample by hybridizing a complementary DNA of mRNA transcribed from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in the sample.

Nor is Hunt *et al.* reasonably pertinent to the particular problem that the present inventors faced. Hunt *et al.* addresses the "sequence requirements for the polyadenylation of mRNAs in plants." Hunt, *et al.*, at page 329. A person faced with the problem of

detecting the expression of a first transgenic nucleic acid molecule would not find the teachings of Hunt pertinent.

Moreover, Freeman *et al.* does not make up what Hunt lacks. The Examiner argues that Freeman *et al.* "teaches designing primers for use in [quantitative RT-PCR assays] to be gene specific or non-specific however if specific then it 'increases specificity and decreases background associated with other types of primers.'" Office Action at page 11. Applicants submit that Freeman *et al.* further describe non-specific primers as "[r]andom hexamer primers [containing] all possible nucleotide combinations of a 6-base oligonucleotide and bind to all RNAs present," and "oligonucleotides solely of deoxythymidine residues [oligo(dT)]." Freeman, *et al.* at page 113. The cited references do not disclose a method for detecting the expression of a first transgenic nucleic acid molecule in a sample by hybridizing a complementary DNA of mRNA transcribed from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in the sample.

In sum, the Examiner's conclusion of obviousness is based on improper hindsight reasoning. "Impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." M.P.E.P. § 2142 at 2100-124. No suggestion to modify the cited references has been found in the cited references or pointed out to Applicant from the general knowledge of one of ordinary skill in the art. In addition, no indication for Hunt *et al.* teaching the claimed method is provided. For at least these reasons, the Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness, as required by 35 U.S.C. § 103.

Accordingly, for at least the foregoing reasons, the rejection of claims 35-50 under 35 U.S.C. § 103 is improper and should be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,

Date: May 6, 2005

Thomas E. Holsten (Reg. No. 46,098)
David R. Marsh (Reg. No. 41,408)

ARNOLD & PORTER LLP
555 Twelfth Street, NW
Washington, DC 20004-2402
(202) 942-5000 telephone
(202) 942-5999 facsimile

Of Counsel
Lawrence M. Lavin, Jr. (Reg. No. 30,768)
Thomas E. Kelley (Reg. No. 29,938)
Monsanto Company

APPENDIX A

Claims as Pending

Claims 1-34. (Cancelled)

35. A method to detect expression of a first transgenic nucleic acid molecule in a sample having either (a) a detectable amount of mRNA transcribed from a second transgenic nucleic acid molecule or (b) a substantially non-detectable amount of said mRNA, said method comprising providing a complementary DNA of the mRNA, amplifying said complementary DNA and hybridizing said complementary DNA with at least one oligonucleotide designed to hybridize to said second transgenic nucleic acid molecule whereby said hybridizing indicates the expression of said first transgenic nucleic acid molecule in a sample.

36. A method according to claim 35 further comprising quantitation of mRNA transcribed from said second transgenic nucleic acid molecule.

37. A method according to claim 35 wherein said second transgenic nucleic acid molecule which is selected from the group consisting of signal sequences, 3' UTR sequences and 5' UTR sequences.

38. A method according to claim 35 wherein said second transgenic nucleic acid molecule is a 3' untranslated sequence from the 3' end of the *Pisum sativum* rbcS E9 gene.

39. A method according to claim 35 wherein said second transgenic nucleic acid molecule has a sequence of SEQ ID NO: 2.

40. A method according to claim 35 wherein the at least one oligonucleotide is a sequence which is a molecule selected from the group consisting of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 28.

41. A method according to claim 35 wherein the amplifying is carried out by a method selected from the group consisting of PCR or RT-PCR.

42. A method according to claim 36 wherein the quantitation of mRNA is determined by a method selected from the group consisting of quantitative RT-PCR or competitive quantitative RT-PCR.

43. A method according to claim 35 wherein said second transgenic nucleic acid molecule comprises at least 100 base pairs of consecutive sequence having a sequence of SEQ ID NO: 2.

44. A method according to claim 35 wherein at least one oligonucleotide comprises at least 15 bases from or complementary to a consecutive sequence of SEQ ID NO: 2.

45. A method according to claim 35 wherein at least one oligonucleotide has a detectable label.

46. A method according to claim 45 wherein said label is selected from the group consisting of a fluorescent label, a digoxigenen-dUTP label, a biotin label, and a radiolabel.

47. A method according to claim 35 wherein said at least one oligonucleotide comprises a pair of oligonucleotide primers and an oligonucleotide probe designed to hybridize to said second transgenic nucleic acid molecule in a 5' nuclease assay.

48. A method according to claim 47 wherein each of said primer pair used in said amplification comprises 15 to 30 bases identical or complementary to a consecutive sequence of a second transgenic nucleic acid molecule having a sequence selected from the group consisting of signal sequences, 3' UTR sequences and 5' UTR sequences and wherein said probe comprises 15 to 30 bases complementary or identical to a second transgenic nucleic acid molecule having a sequence selected from the group consisting of signal sequences, 3' UTR sequences and 5' UTR sequences.

49. A method according to claim 35 further comprising Southern Blotting, Northern Blotting or RNAse protection assay.

50. An amplification kit for the detection of a transgenic nucleic acid molecule comprising at least one primer pair and a corresponding labeled probe which hybridizes under stringent hybridization conditions to a nucleic acid molecule of a 3' end of the *Pisum sativum* rbcS E9 gene.